

CLAIMS

1. A method of nucleic acid transfer comprising the following steps (a) and (b):

- 5 (a) contacting a nucleic acid with a cell in a medium; and
(b) following the step (a), contacting the medium of (a) with a high-concentration solution of a metal salt.

2. The method of nucleic acid transfer according to claim 1, wherein the nucleic acid is a single-stranded DNA, a double-stranded DNA,
10 a single-stranded RNA, a double-stranded RNA, an oligonucleotide or a ribozyme.

3. The method of nucleic acid transfer according to claim 2, wherein the double-stranded DNA or the double-stranded RNA is in the linear or cyclic form.

15 4. The method of nucleic acid transfer according to claim 3, wherein the cyclic double-stranded DNA is in the form of expression plasmid.

5. The method of nucleic acid transfer according to claim 2, wherein the oligonucleotide is a deoxyribonucleotide, a ribonucleotide, a
20 phosphorothioate oligodeoxynucleotide, a 2'-O-(2-methoxy)ethyl-modified nucleic acid (2'-MOE-modified nucleic acid), a small interfering RNA (siRNA), a cross-linked nucleic acid (locked nucleic acid; LNA), a peptide nucleic acid (PNA) or a morpholino antisense nucleic acid.

6. The method of nucleic acid transfer according to any one of
25 claims 1 to 5, wherein the nucleic acid is in the form of a complex or an inclusion body with a biodegradable substance or a living body-derived substance.

7. The method of nucleic acid transfer according to claim 6, wherein the living body-derived substance is atelocollagen.

30 8. The method of nucleic acid transfer according to any one of

claims 1 to 7, wherein the concentration of the high-concentration solution of a metal salt to be contacted with the medium obtained in the step (a) is within the range of 0.1 M - 3.0 M.

5 9. The method of nucleic acid transfer according to claim 8, wherein the concentration of the high-concentration solution of a metal salt to be contacted with the medium obtained in the step (a) is within the range of 0.5 M - 2.0 M.

10 10. The method of nucleic acid transfer according to any one of claims 1 to 9, wherein the volume of the high-concentration solution of a metal salt to be contacted with the medium obtained in the step (a) is within the range of 1 μ L - 20 μ L per 500 μ L of the medium of step (a).

15 11. The method of nucleic acid transfer according to claim 10, wherein the volume of the high-concentration solution of a metal salt to be contacted with the medium obtained in the step (a) is within the range of 2 μ L - 10 μ L per 500 μ L of the medium of step (a).

12. The method of nucleic acid transfer according to any one of claims 1 to 11, wherein the solution of a metal salt is a solution of a divalent metal chloride.

20 13. The method of nucleic acid transfer according to claim 12, wherein the solution of a divalent metal chloride is a solution of calcium chloride.

14. A nucleic acid transfer agent comprising a solid metal salt or a high-concentration solution of a metal salt as an ingredient.

25 15. The nucleic acid transfer agent according to claim 14, which is used in the method of nucleic acid transfer set forth in any one of claims 1 to 13.

16. The nucleic acid transfer agent according to claim 14 or 15, wherein the concentration of the high-concentration solution of a metal salt is within the range of 0.1 M - 6.0 M.

30 17. The nucleic acid transfer agent according to claim 16, wherein

the concentration of the high-concentration solution of a metal salt is within the range of 0.5 M - 4.0 M.

18. The nucleic acid transfer agent according to any one of claims 14 to 17, wherein the metal salt is a chloride of divalent metal.

5 19. The nucleic acid transfer agent according to 18, wherein the chloride of a divalent metal is calcium chloride.

20. A kit for nucleic acid transfer which comprises a nucleic acid transfer agent set forth in any one of claims 14 to 19.

10 21. Use of a nucleic acid transfer agent or a kit set forth in any one of claims 14 to 20 in the nucleic acid transfer.